

Amendments to the Claims

Please amend the claims as follows. This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

The following list of claims represents the current claim status for all claims:

1. (Withdrawn) A subtelomeric probe useful for detecting chromosomal rearrangements comprising:
a single copy DNA sequence having a length of less than 25 kb, said sequence being capable of hybridizing to the terminal G-band or R-band of an arm of a single chromosome.
2. (Withdrawn) The probe of claim 1, said terminal band being light after G-band staining.
3. (Withdrawn) The probe of claim 1, said terminal band being dark after R-band staining.
4. (Withdrawn) The probe of claim 1, said arm of said single chromosome being selected from the group consisting of 1p, 1q, 2p, 2q, 3p, 3q, 4p, 4q,

5p, 5q, 6p, 6q, 7p, 7q, 8p, 8q, 9p, 9q, 10p, 10q, 11p, 11q, 12p, 12q, 13q, 14q, 15q, 16p, 16q, 17p, 17q, 18p, 18q, 19p, 19q, 20p, 20q, 21q, 22q, Xp, Xq, and Yp.

5. (Withdrawn) The probe of claim 1, said probe being selected from the group consisting of SEQ ID NOS. 1- 3, 5-23, 26-36, 38-57, 59-61, 63-67, 69-82, and 245-251.

6. (Withdrawn) The probe of claim 1, said probe having a length of less than 10 kb.

7. (Withdrawn) The probe of claim 1, said probe being within 8000 kb of the telomere of said chromosome.

8. (Withdrawn) The probe of claim 7, said probe being selected from the group consisting of SEQ ID NOS. 1- 3, 5-23, 26-36, 38-57, 59-61, 63-67, 69-82, and 245-251

9. (Withdrawn) The probe of claim 1, said probe being within 300 kb of the telomere of said chromosome.

10. (Withdrawn) The probe of claim 9, said probe being selected from the group consisting of SEQ ID NOS. 36, 80, 46, 47, 49, 51, 56, 248, 57, 78, 59, 75,

76, 74, 63, 250, 251, 66, 65, 67, 4, 3, 1, 9, 6, 11, 10, 17, 20, 19, 18, 21, 81, 26, 29, 28, 31, 32, 43, 42, 41, 40, 44, 45, and 70.

11. (Withdrawn) The probe of claim 1, said probe being labeled or being modified to attach to a surface.

12. (Withdrawn) A method of developing single copy DNA sequence probes from subtelomeric regions of chromosomes, said probes being able to hybridize to a single location in the genome, said method comprising the steps of:

searching the DNA sequence of said chromosome on a nucleotide-by-nucleotide basis beginning at the terminal nucleotide for a single copy interval of at least 500 base pairs in length that is closest to said terminal nucleotide;

identifying said single copy interval;

synthesizing said single copy interval; and

using said synthesized single copy interval as said probes.

13. (Withdrawn) The method of claim 12, said identifying step including the step of verifying computationally or experimentally that said identified single copy interval is represented at a single genomic location or where paralogous sequences are closely linked so that only a single signal is detected.

14. (Withdrawn) The method of claim 13, said identifying step including verifying computationally and experimentally.

15. (Withdrawn) The method of claim 13, said computational verification including using software to determine that the probe sequence is located at a single position in the genome.

16. (Withdrawn) The method of claim 12, said method further including the step of labeling said synthesized single copy sequence.

17. (Withdrawn) The method of claim 13, said experimental verification including rehybridizing said single copy probe to said chromosome and visualizing said probe on the terminal band and correct arm of said chromosome.

18. (Withdrawn) The method of claim 12, said single copy interval being selected from the group consisting of SEQ ID NOS. 1- 3, 5-23, 26-36, 38-57, 59-61, 63-67, 69-82, and 245-251.

19. (Withdrawn) The method of claim 12, said method further comprising the step of preannealing said single copy probe with highly repetitive DNA.

20. (Withdrawn) A synthetic single copy polynucleotide for identifying chromosomal rearrangements, said polynucleotide being located within 8,000 kb of the terminal nucleotide of a chromosome and hybridizing to a single location on a

specific chromosome when no chromosomal rearrangement has occurred, said polynucleotide having a length of less than 25 kb.

21. (Withdrawn) The polynucleotide of claim 20, said polynucleotide being found in the terminal G-band or R-band of said specific chromosome.

22. (Withdrawn) The polynucleotide of claim 20, said polynucleotide being selected from the group consisting of SEQ ID NOS. 1- 3, 5-23, 26-36, 38-57, 59-61, 63-67, 69-82, and 245-251.

23. (Withdrawn) The polynucleotide of claim 20, said polynucleotide being located within about 300 kb of said terminal nucleotide of said specific chromosome.

24. (Withdrawn) The polynucleotide of claim 23, said polynucleotide being selected from the group consisting of SEQ ID NOS. 36, 80, 46, 47, 49, 51, 56, 248, 57, 78, 59, 75, 76, 74, 63, 250, 251, 66, 65, 67, 4, 3, 1, 9, 6, 11, 10, 17, 20, 19, 18, 21, 81, 26, 29, 28, 31, 32, 43, 42, 41, 40, 44, 45, and 70.

25. (Withdrawn) The polynucleotide of claim 20, said polynucleotide being labeled or being chemically modified to attach to a surface.

26. (Withdrawn) An oligonucleotide primer pair used for deriving single copy probes that can detect chromosomal rearrangements, said primers comprising:

a sequence selected from the group consisting of SEQ ID NOS. 83-244.

27. (Withdrawn) An improved synthetic DNA probe operable for detecting chromosomal rearrangements, said probe including a DNA sequence operable to hybridize to a precise location on a single chromosome arm wherein the improvement comprises a probe of less than 25 kb in length.

28. (Withdrawn) The improved probe of claim 27, said portion comprising the entire probe.

29. (Withdrawn) The improved probe of claim 27, said probe having at least a portion thereof being located closer to the end of a telomere on a chromosome arm than a clone selected from the group consisting of cosmids, fosmids, bacteriophage, P1, and PAC clones derived from half YACS, said chromosome arm being selected from the group consisting of 2p, 3p, 5p, 7p, 8p, 10p, 11p, 12p, 16p, 17p, 18p, Xp, Yp, 1q, 3q, 4q, 6q, 7q, 8q, 9q, 10q, 11q, 12q, 13q, 14q, 15q, 16q, 17q, 18q, 19q, 20q, 21q, and 22q.

30. (Withdrawn) The improved probe of claim 27, said probe being located within 8,000 kb of the terminal nucleotide of the telomere of said chromosome.

31. (Withdrawn) The improved probe of claim 27, said probe being located within 300 kb of the terminal nucleotide of the telomere of said chromosome.

32. (Withdrawn) The improved probe of claim 27, said probe being located in the terminal G-band or R-band of said chromosome.

33. (Withdrawn) The improved probe of claim 27, said probe being selected from the group consisting of SEQ ID NOS. 46, 47, 49, 56, 78, 59, 64, 249, 2, 4, 3, 5, 9, 11, 20, 19, 21, 81, 246, 70, 72, 73, 36, 80, 247, 50, 57, 75, 76, 74, 63, 250, 66, 65, 67, 1, 6, 10, 12, 16, 15, 13, 14, 17, 18, 81, 245, 26, 31, 32, 43, 42, 41, 40, 44, and 45.

34 -42. (Cancelled)

43. (Currently Amended) A method of screening at least one chromosome of a human for cytogenetic abnormalities, said method comprising the steps of:

screening the at least one chromosome of a human using a plurality of single-copy hybridization probes of known human DNA sequence, each of said single copy probes being between 25 bp to about 15 kb in length;

causing said single copy probes to hybridize to the at least one chromosome of the human using a conventional FISH protocol,

said hybridization occurring within 600kb of the terminal nucleotide of the at least one chromosome; and detecting hybridization patterns of said single copy probes, said hybridization patterns indicating cytogenetic abnormalities when they are present in said chromosome.

44. (Previously Presented) The method of claim 43, said method further including the step of associating said hybridization patterns with specific clinical abnormalities.

45. (Previously Presented) The method of claim 43, said single-copy probes being represented at a single genomic location or where paralogous sequences are closely linked so that only a single hybridization signal is detected.

46. (Currently Amended) The method of claim 43, each of said plurality of single copy probes having a known sequence.

47. (Currently Amended) The method of claim 43, each of said plurality of single copy probes having a length between 50 bp and 12 kb.

48. (Previously Presented) The method of claim 43, wherein said cytogenetic abnormalities are correlated with a medical condition selected from the group

consisting of idiopathic mental retardation, or mental retardation and at least one other clinical abnormality, or mental retardation and cancer, or combinations thereof.

49. (Currently Amended) A method of delineating the extent of a chromosome imbalance in a human individual comprising the steps of:

assaying a subtelomeric region of a human chromosome arm using at least one single-copy hybridization probe of known sequence located within 600 kb of the terminal nucleotide of the chromosome arm said single copy probe being comprised of human DNA;

hybridizing said single copy probe with said region using a conventional FISH protocol;

detecting hybridization patterns of said single copy probes on said arm; and comparing said hybridization patterns with a standard genome map of said arm in order to delineate the extent of a chromosome imbalance.

50. (Previously Presented) The method of claim 49, said method further including the step of correlating imbalances on said arm with a medical condition of the individual, said individual being capable of having said medical condition, said medical condition being selected from the group consisting of idiopathic mental retardation or cancer applicable to those individuals capable of experiencing idiopathic mental retardation.

51. (Currently Amended) The method of claim 49, said method utilizing a plurality of single copy probes.

52. (Currently Amended) The method of claim 49, said single copy probe hybridizing to a specific chromosome arm.

53. (Cancelled)

54. (Currently Amended) The method of claim 49, said single copy probe having a length of between 50 bp and 12 kb.